

**THE AMENDMENT**

**In the Claims:**

1. (Currently Amended) A method for discriminating metaplasias from neoplastic lesions in a biological sample in the course of cytological testing procedures comprising:
  - a. determining the presence ~~or absence~~ of cells overexpressing at least one INK4a gene-product in said biological sample;
  - b. determining the presence ~~or absence~~ of cells expressing at least one different INK4a gene-product in said biological sample;
  - c. ~~assessing simultaneous presence of cells expressing two different INK4a gene-products or the presence of cells overexpressing only one INK4a gene-product alone;~~
  - d. wherein in said biological sample, the simultaneous presence of cells expressing at least two different INK4a gene-products overexpressing the one INK4a gene-product and cells expressing the one different INK4a gene-product is indicative for neoplastic lesions, wherein said one INK4a gene-product or one different INK4a gene product is a polypeptide.
2. (Previously Presented) The method according to claim 1, wherein said at least one INK4a gene-product or said at least one different INK4a gene-product has a molecular weight between 13 and 19 kDa.
3. (Previously Presented) The method according to claim 1, wherein said at least one INK4a gene-product is p16<sup>INK4a</sup>.
4. (Previously Presented) The method according to claim 1, wherein at least one different INK4a gene-product is p14ARF.
5. (Canceled)
6. (Previously Presented) The method according to claim 1, wherein the neoplastic lesions are lesions of the anogenital tract.
7. (Original) The method according to claim 6, wherein the lesion of the anogenital tract is a lesion of the uterine cervix.

8. (Previously Presented) The method according to claim 1, wherein the biological sample is a sample containing cells of anogenital origin.
9. (Previously Presented) The method according to claim 8, wherein the cells are cells originating from the uterine cervix.
10. (Previously Presented) The method according to claim 9, wherein the biological sample is a cytological or histological preparation of the cervix uteri.
11. (Previously Presented) The method according to claim 1, wherein the determination of the INK4a gene-products is performed using at least one probe specifically recognizing the INK4a gene-products.
12. (Previously Presented) The method according to claim 11, wherein the probe is detectably labelled.
13. (Previously Presented) The method according to claim 12, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, or an enzyme.
14. (Currently Amended) The method according to claim 11, wherein the probe is a polypeptide ~~or a nucleic acid~~.
15. (Previously Presented) The method according to claim 14, wherein the probe is an antibody directed against an INK4a encoded gene-product.
16. (Previously Presented) The method according to claim 15, wherein the determination of the INK4a gene-products comprises an immuno-cytochemical staining procedure.
- 17-20. (Canceled)
21. (Withdrawn) The method according to claim 14, wherein the determination of the INK4a gene-products is performed using nucleic acid probes and polypeptide probes simultaneously.
22. (Withdrawn) A diagnostic kit or a research kit, comprising at least one or more probes for detecting the presence or absence and/or the level of the overexpression of two or more INK4a gene-products in biological samples.

23. (Withdrawn) The diagnostic or research kit according to claim 22, wherein the INK4a gene products are selected from the group consisting of p16<sup>INK4a</sup> and p14ARF.

24. (Withdrawn) The diagnostic or research kit according to claim 23, furthermore comprising at least one of the following:

- a. a p16<sup>INK4a</sup> sample for carrying out a positive control reaction,
- b. a p14ARF sample for carrying out a positive control reaction,
- c. reagents for detection of the presence or absence and/or the level of p16<sup>INK4a</sup>,
- d. reagents for detection of the presence or absence and/or the level of p14ARF,
- e. one or more samples of INK4a gene-products for carrying out positive control reactions, and
- f. and one or more reagents for the detection of the presence or absence and/or the level of other INK4a gene products.

25. (Withdrawn) An immunogenic peptide derived from a cell cycle regulatory protein encoded by an alternative reading frame of the INK4a gene locus.

26. (Withdrawn) The immunogenic peptide according to claim 25 selected from the group consisting of:

- a. a peptide from the amino acid sequence of the cell cycle regulatory protein;
- b. an HLA-A3 restricted nonamer peptide;
- c. an HLA-A2 restricted nonamer peptide;
- d. an HLA-A\*0201 restricted nonamer peptide; and
- e. a 15-mer peptide.

27. (Withdrawn) The immunogenic peptide according to claim 26, wherein the peptide is selected from the group consisting of SEQ IDs No. 1-23.

28. (Withdrawn) A method of treating tumors comprising the steps of administering to a subject in need thereof a pharmaceutical composition comprising one or more

immunogenic peptides derived from a cell cycle regulatory protein encoded by an alternative reading frame of the INK4a gene locus.

29. (Withdrawn) The method according to claim 28, wherein the treatment is selected from the group consisting of curative and preventive immunotherapy.
30. (Withdrawn) The method according to claim 29, wherein the immunotherapy is vaccination therapy.
31. (Withdrawn) The method according to claim 28, wherein the tumors are selected from the group consisting of benign or malignant tumors, carcinomas, sarcomas, leukemias, lymphomas and dysplasias.
32. (Withdrawn) The method according to claim 31, wherein the tumors are selected from the group consisting of cervical cancer, lung cancer, gastric cancer, and colon cancer.
33. (Withdrawn) The method according to claim 28, further comprising administering to the subject one or more other peptides derived from tumor associated proteins.
34. (Withdrawn) A binding agent directed against the immunogenic peptide according to claim 25, selected from the group consisting of:
  - a. a monoclonal antibody;
  - b. a mini-antibody;
  - c. an antigen binding fragment;
  - d. an antigen binding peptidomimetic molecule; and
  - e. a polyclonal antibody .
35. (Withdrawn) A pharmaceutical composition comprising one or more peptides according to claim 25 and/or one or more binding agents according to claim 34.
36. (Withdrawn) The pharmaceutical composition according to claim 35, further comprising one or more additional peptides derived from proteins, which show non wild-type expression in tumors.

37. (Withdrawn) The pharmaceutical composition according to claim 36, wherein the additional peptides are derived from proteins selected from the group consisting of p16<sup>INK4a</sup>, HPV E6, HPV E7, HPV E2 HPV E4, HPV L1, HPV L2, p27, p21, p15, p19, p53, pRb, and MDM2.
38. (Withdrawn) A method for detecting immunological entities specifically recognizing the immunogenic peptide according to claim 25 in individuals comprising the steps of
- a. obtaining a sample from the individual;
  - b. contacting the sample with a binding agent binding to said immunological entities selected from the group consisting of:
    - i. a binding agent directed against said immunological entities,
    - ii. a binding agent directed against complexes of the immunological entities together with the respective immunogenic peptides,
    - iii. at least one peptide according to claim 25,wherein said contacting is performed in a way, that binding of the immunological entities to said binding agents gives rise to a detectable signal; and
  - c. assessing the presence or absence and/or the level of immunological entities in said sample from the presence or absence and/or the level of detectable signal.
39. (Withdrawn) The method according to claim 38, which is used for purposes selected from the group consisting of:
- a. monitoring in the course of a therapy using peptides according to claim 1;
  - b. monitoring in the course of the application of a pharmaceutical composition according to claim 35; and
  - c. monitoring in the course of the method according to claim 28.
40. (Withdrawn) The method according to claim 38, which is used for the diagnosis and monitoring of the disease course of tumors.

41. (Withdrawn) The method according to claim 38, wherein the sample is selected from the group consisting of secretions, smears, body fluids, serum, blood, plasma, urine, semen, stool, bile, sputum, biopsies, cell- and tissue-samples, resection samples of tumors, tissue samples prepared by endoscopic means and needle biopsies of organs.
42. (Withdrawn) A diagnostic kit or a research kit, comprising one or more immunogenic peptides derived from a cell cycle regulatory protein encoded by an alternative reading frame of the INK4a gene locus or one or more binding agents directed against said immunogenic peptides.
43. (Canceled).